

BMJ Open Association of sleep duration with rheumatoid arthritis in Korean adults: analysis of seven years of aggregated data from the Korea National Health and Nutrition Examination Survey (KNHANES)

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ABSTRACT

Objectives: To investigate the association between rheumatoid arthritis (RA) and self-reported sleep duration.

Setting: The present study analysed 7 years of aggregated cross-sectional data (2007–2013) from the Korea National Health and Nutrition Examination Surveys (KNHANES).

Participants: A total of 37 979 individuals were selected for the analyses.

Interventions: RA.

Primary and secondary outcome measures: Sleep duration.

Results: After adjusting for confounding factors, the odds of short-duration sleepers (≤ 6 hours/day) and long-duration sleepers (≥ 9 hours/day) for RA were 1.23-fold (95% CI 1.101 to 1.51) and 1.27-fold (95% CI 0.85 to 1.88) higher, respectively, than those for persons with sleep duration of 7–8 hours/day. A subgroup analysis according to the extent of pain in RA revealed that the strong relationship between RA and sleep disturbances was observed in those with high pain from RA (OR: 1.28 CI 1.04 to 1.58).

Conclusions: Individuals with RA may be at a higher risk for sleep disturbances compared with individuals without RA. Therefore, the provision of comprehensive care for patients with RA by healthcare professionals should include assessments of sleep duration and patients with RA should be encouraged to report sleep problems.

INTRODUCTION

Arthritis is the most common cause of disability worldwide. Rheumatoid arthritis (RA) is characterised by persistent inflammatory symmetrical synovitis with pain, swelling and a broad range of systemic manifestations in

Strengths and limitations of this study

- This study used nationwide survey data of community dwelling people. A large population sample size was representative of the general population, so that the results can be generalised to the general population in South Korea.
- The lack of validated questionnaires assessing rheumatoid arthritis and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results.
- Respondents' reports were subjective and were imperfect measures potentially affected by perception bias and adaptation of resources.
- We used cross-sectional nature data for our estimates. Therefore, the results possibly reflected reverse causality and are bidirectional.

the peripheral joints.¹ This disease is also associated with sleep disturbances² which play an important role in the maintenance of an individual's health.^{3–4} Importantly, poor sleep in patients with RA could originate from pain or may contribute to increased level of pain and fatigue.^{5–6} Additionally, sleep disorders such as sleep apnoea or primary insomnia typically result in poor sleep quality in patients with RA as well as exacerbating the patient's primary symptoms.⁷

Sleep disturbances affect more than half of patients with RA^{8–9} and are thought to be more common among those with active inflammation¹⁰ or physical health conditions such as associated pain, fatigue and/or functional disabilities.¹¹ Although physicians often assume that inflammation is the stimulus for RA-related pain, many of these

patients continue to experience pain following adequate suppression of inflammation.¹² Furthermore, sleep disturbances and inadequate sleep are related to serious outcomes such as reduced health-related quality of life,¹³ a higher risk of morbidities¹⁴ and, ultimately, increase in all-cause mortality.¹⁵ Additionally, sleep disturbances are almost threefold more frequent in females than males.¹⁶ Thus, the quality and amount of sleep in patients with RA are important issues for rheumatologists, particularly after the finding that etanercept and infliximab's ability to reduce daytime sleepiness.¹⁷

Therefore, the primary aim of the present study was to investigate the association between RA and self-reported sleep duration using 7 years of aggregated cross-sectional data (2007–2013) obtained from the Korea National Health and Nutrition Examination Survey (KNHANES).

METHODS

Study sample

To evaluate the relationship between sleep duration and RA, the present study analysed data from the fourth (2007–2009), fifth (2010–2012) and sixth (2013) KNHANES assessments performed by the Korean Ministry of Health and Welfare. The KNHANES is a cross-sectional survey based on stratified multistage probability sampling units of Korean households that targets members of the civilian non-institutionalised South Korean population who are 1-year of age or older. The samples were determined by the household registries of the 2005 National Census Registry.

The total target population initially consisted of 24 871, 25 534 and 8018 participants who completed the 2007–2009, 2010–2012 and 2013 KNHANES assessments, which had average response rates of 78.4%, 80.8% and 79.3%, respectively. The information from 14 305 individuals aged 1–18 years old were excluded from the present analyses while the information of 44 118 individuals aged 19 years and older were included. Additionally, the present study excluded 6036 individuals with missing data regarding age, occupation, income and/or marriage status and 103 individuals with missing data regarding smoking, drinking, perceived stress, exercise, sleep duration, RA, hypertension, and/or dyslipidaemia. Thus, a total of 37 979 individuals were selected for the final analyses in the present study. Since all KNHANES data are available publicly, this study did not require approval from an institutional review board.

Variables

Dependent variables

In the present study, sleep duration was based on self-reported data acquired in response to the question 'How many hours do you usually sleep?'. The responses were classified into three categories (≤ 6 hours, 7–8 hours and ≥ 9 hours) based on the sleep definitions of the International Classification of Sleep Disorders,

2nd edition, in which ≤ 6 hours is defined as a short sleeper and ≥ 9 hours as a long sleeper.¹⁸

Independent variables

In the present study, diabetes mellitus type 2 cases were considered to be the participants who answered 'Yes' to the question 'Are you currently suffering from RA?' in the self-reported data. RA was categorised as either 'Yes' or 'No'.

Sociodemographic factors

The present analyses included age, gender, household income, marital status, occupation and region of residency as sociodemographic factors; all of the covariates were categorical. Individual income was calculated by dividing a participant's household monthly income by the square root of the household size, and the participants were ranked from lowest to highest income and then grouped into four household income quartiles. Predefined categories were used to categorise household incomes, similar to how the raw KNHANES data are processed. The residency regions were categorised into urban (administrative divisions of a city: Seoul, Daejeon, Daegu, Busan, Incheon, Kwangju or Ulsan) and rural (not classified as administrative of a city), and occupational status was classified into the following three categories: white collar (administrative, engineering, scientific, teaching and related occupations, sales and related occupations, and service occupation), blue collar (farming, forestry, fishing and hunting, craft and repair, operators, fabricators, and labourers) and unpaid employment (including housewives and students).

Health behaviour factors

Questions regarding alcohol use, smoking status and the number of days of moderate exercise per week were assessed by a health interview survey and included as covariates in the present analyses. Alcohol use was further assessed by questioning the participants about their average frequency (days per week or month) of alcohol use during the past year.

Health status factors

Perceived stress, the extent of RA pain and body mass index (BMI) were also included in the present model. The following were categorised into four groups for the present analyses: perceived stress (very high, high, low and very low), and BMI (thin: $<18.5 \text{ kg/m}^2$, moderate: $18.5\text{--}23.9 \text{ kg/m}^2$, overweight: $24.0\text{--}26.9 \text{ kg/m}^2$ and obese: $>27.0 \text{ kg/m}^2$).¹⁹ Extent of RA pain was measured by asking the respondents to assess the extent suffering from RA using a pictorial representation of 0–10 scores. Extent of RA pain was categorised into two groups: Low (0–5) or High (6–10).

Statistical analysis

The distributions of the general characteristics of the participants were assessed using χ^2 tests, and

Table 1 Demographic characteristics of the study population

	Sleep duration								p Value
	Total		Short sleeper (≤6 hours)		Appropriate sleeper (7–8 hours)		Long sleeper (≥9 hours)		
	N	Per cent	N	Per cent	N	Per cent	N	Per cent	
Rheumatoid arthritis (RA)									<0.0001
No	37 309	98.2	15 508	40.8	18 883	49.7	2918	7.7	
Yes	670	1.8	347	51.8	58	8.7	265	39.6	
Age (year)									<0.0001
≤29	4751	12.5	1566	33.0	2569	54.1	616	13.0	
30–49	14 551	38.3	5476	37.6	8259	56.8	816	5.6	
50–69	13 135	34.6	6001	45.7	6253	47.6	881	6.7	
≥79	5542	14.6	2812	50.7	2067	37.3	663	12.0	
Gender									<0.0001
Male	16 254	42.8	6732	41.4	8357	51.4	1165	7.2	
Female	21 725	57.2	9123	42.0	10 791	49.7	1811	8.3	
Household income level									<0.0001
Low	7633	20.1	3592	47.1	3226	42.3	815	10.7	
Lower middle	9685	25.5	4102	42.4	4790	49.5	793	8.2	
Upper middle	10 216	26.9	3980	39.0	5462	53.5	774	7.6	
High	10 445	27.5	4181	40.0	5670	54.3	594	5.7	
Marital status									<0.0001
Married	27 602	72.7	11 246	40.7	14 338	52.0	2018	7.3	
Single	5312	14.0	1889	35.6	2876	54.1	547	10.3	
Separated, divorced	5065	13.3	2720	53.7	1934	38.2	411	8.1	
Occupation									<0.0001
White collar	12 635	33.3	5171	40.9	6846	54.2	618	4.9	
Blue collar	10 340	27.2	4488	43.4	5073	49.1	779	7.5	
Unpaid employment	15 004	39.5	6196	41.3	7229	48.2	1579	10.5	
Residential region									<0.0001
Urban	17 032	44.9	7363	43.2	8517	50.0	1152	6.8	
Rural	20 947	55.2	8492	40.5	10 631	50.8	1824	8.7	
Smoking status									0.402
Current smoker	11 101	29.2	4564	41.1	5633	50.7	904	8.1	
Former smoker	4552	12.0	1927	42.3	2280	50.1	345	7.6	
Never smoked	22 326	58.8	9364	41.9	11 235	50.3	1727	7.7	
Frequency of alcohol use									<0.0001
Never drink	10 950	28.8	4947	45.2	5018	45.8	985	9.0	
1 times or less per month	10 786	28.4	4238	39.3	5734	53.2	814	7.6	
2–4 times per week	13 510	35.6	5462	40.4	7122	52.7	926	6.9	
4 times or more per week	2733	7.2	1208	44.2	1274	46.6	251	9.2	
Number of days of moderate exercise per week									<0.0001
Never	23 187	61.1	9718	41.9	11 457	49.4	2012	8.7	
1–3	9145	24.1	3741	40.9	4829	52.8	575	6.3	
4–6	3318	8.7	1361	41.0	1761	53.1	196	5.9	
Everyday	2329	6.1	1035	44.4	1101	47.3	193	8.3	
Perceived stress									<0.0001
Very high	1749	4.6	920	52.6	685	39.2	144	8.2	
High	8442	22.2	3960	46.9	3887	46.0	595	7.1	
Low	21 556	56.8	8495	39.4	11 480	53.3	1581	7.3	
Very low	6232	16.4	2480	39.8	3096	49.7	656	10.5	
Extent of pain from RA									<0.0001
Low	36 660	96.5	15 099	41.2	18 708	51.0	2853	7.8	
High	1319	3.5	756	57.3	440	33.4	123	9.3	

Continued

Table 1 Continued

	Sleep duration								p Value
	Total		Short sleeper (≤6 hours)		Appropriate sleeper (7–8 hours)		Long sleeper (≥9 hours)		
	N	Per cent	N	Per cent	N	Per cent	N	Per cent	
BMI									<0.0001
Thin (<18.5 kg/m ²)	1908	5.0	656	34.4	1010	52.9	242	12.7	
Moderate (18.5kg/m-23.9kg/m ²)	19 689	51.8	7970	40.5	10 153	51.6	1566	8.0	
Overweight (24.0kg/m-26.9kg/m ²)	10 767	28.4	4649	43.2	5351	49.7	767	7.1	
Obese (≥27.0 kg/m ²)	5615	14.8	2580	46.0	2634	46.9	401	7.1	
Year									<0.0001
2007	1403	3.7	576	41.1	747	53.2	80	5.7	
2008	6513	17.2	2672	41.0	3258	50.0	583	9.0	
2009	7338	19.3	2922	39.8	3796	51.7	620	8.5	
2010	6059	16.0	2461	40.6	3114	51.4	484	8.0	
2011	5927	15.6	2535	42.8	2947	49.7	445	7.5	
2012	5465	14.4	2303	42.1	2762	50.5	400	7.3	
2013	5274	13.9	2386	45.2	2524	47.9	364	6.9	
Total	37 979	100.0	15 855	41.8	19 148	50.4	2976	7.8	

BMI, body mass index.

multinomial logistic regression analyses were used to determine whether the general characteristics, health statuses and/or health risk behaviours of the participants had relationships with RA. All data were analysed using SAS software, V.9.4 (SAS Institute; Cary, North Carolina, USA).

RESULTS

Prevalence of short sleep and long sleep durations

Of the 37 979 KNHANES participants included in the present study, 16 254 were men (42.8%), 21 735 were women (57.2%) and 670 were patients with RA (1.8%). Of the 15 855 participants who reported a short sleeper (≤6 hours), 347 had RA (51.8%), while of the 2976 participants who reported a long sleeper (≥9 hours), 265 had RA (39.6%; [table 1](#)).

Association between sleep duration and RA

[Table 2](#) portrays the results of the logistic regression analyses after adjusting for age, gender, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use, number of days of moderate exercise per week, perceived stress, extent of RA pain, BMI and year of the survey. After adjusting for all of these confounding variables, in terms of RA, the odds of short sleep (≤6 hours/day) were 1.23-fold higher (95% CI 1.01 to 1.51) and the odds of long sleep (≥9 hours/day) were 1.27-fold higher (95% CI 0.85 to 1.88) than for those with sleep durations of 7–8 hours/day ([table 2](#)).

[Table 3](#) depicts the results of a subgroup analysis according to the extent of RA pain after adjusting for age, household income, marital status, occupation, region of residence, smoking status, frequency of alcohol use,

number of days of moderate exercise per week, perceived stress, BMI and year of the survey. Those who reported RA were 28% more likely to have short sleep (OR: 1.28, 95% CI 1.04 to 1.58), while those who did not report RA were not more likely to have short sleep (OR: 0.84, 95% CI 0.49 to 1.46), compared with those with reported sleep durations of 7–8 hours ([table 3](#)).

DISCUSSION

Since sleep disturbances may be an important clinical feature for patients with RA, this issue has recently received an increasing amount of attention.^{20 21} Thus, the present study aimed to investigate RA and its relationship with sleep duration using 7 years of aggregated data from a large representative population-based survey conducted in Korea. The present study found an association between RA and the reported symptoms of short sleep duration that was statistically significant (OR: 1.23, 95% CI 1.01 to 1.51) even in the presence of perceived stress, which suggests that stress could be a trigger or signal for an inappropriate sleep duration in patients with RA. In general, there is a U-shaped association between RA and short or long sleep duration, and this similarly shaped relationship was evident in this study. In addition, in a subgroup analysis based on the extent of pain in RA, these associations were statistically significant only in those with high pain from RA. These associations were independent of sociodemographic variables, (eg, age, gender, household income level, marital status, occupation and region of residence), health behaviour variables (eg, smoking status, frequency of alcohol use and number of days of moderate exercise per week), and health status variables (eg, perceived stress, the extent of RA pain, BMI), and year of the survey.

Table 2 Results of logistic regression between rheumatoid arthritis and sleep duration

	RA		
	Appropriate sleeper (7–8 hours) Ref	Short sleeper (≤6 hours) OR 95% CI	Long sleeper (≥9 hours) OR 95% CI
RA			
No	1.00		
Yes		1.23 (1.01 to 1.51)	1.27 (0.85 to 1.88)
Age (year)			
≤29	1.00		
30–49		1.16 (1.04 to 1.31)	0.45 (0.37 to 0.55)
50–69		1.49 (1.32 to 1.69)	0.51 (0.42 to 0.63)
≥79		2.15 (1.85 to 2.50)	0.84 (0.65 to 1.08)
Gender			
Male		1.02 (0.95 to 1.10)	0.64 (0.55 to 0.74)
Female	1.00		
Household income level			
Low		1.04 (0.95 to 1.14)	1.50 (1.27 to 1.77)
Lower middle		1.01 (0.93 to 1.09)	1.25 (1.09 to 1.44)
Upper middle		0.95 (0.89 to 1.02)	1.25 (1.08 to 1.44)
High	1.00		
Marital status			
Married	1.00		
Single		1.11 (1.00 to 1.23)	0.99 (0.82 to 1.21)
Separated, divorced		1.49 (1.37 to 1.62)	0.90 (0.77 to 1.06)
Occupation			
White collar	1.00		
Blue collar		1.05 (0.97 to 1.12)	1.32 (1.14 to 1.54)
Unpaid employment		0.87 (0.81 to 0.93)	1.78 (1.55 to 2.04)
Residential region			
Urban	1.00		
Rural		0.88 (0.83 to 0.94)	1.24 (1.12 to 1.38)
Smoking status			
Current smoker		0.99 (0.92 to 1.08)	1.51 (1.31 to 1.75)
Former smoker		0.95 (0.85 to 1.05)	1.51 (1.26 to 1.81)
Never smoked	1.00		
Frequency of alcohol use			
Never drink		0.96 (0.85 to 1.09)	0.88 (0.71 to 1.09)
1 times or less per month		0.89 (0.79 to 1.01)	0.81 (0.65 to 1.00)
2–4 times per week		0.93 (0.83 to 1.04)	0.79 (0.65 to 0.96)
4 times or more per week	1.00		
Number of days of moderate exercise per week			
Never	1.00		
1–3		0.98 (0.92 to 1.05)	0.75 (0.66 to 0.86)
4–6		0.99 (0.90 to 1.09)	0.70 (0.57 to 0.85)
Everyday		1.09 (0.98 to 1.22)	1.04 (0.84 to 1.28)
Perceived stress			
Very high		1.88 (1.64 to 2.16)	1.19 (0.93 to 1.51)
High		1.57 (1.44 to 1.71)	0.86 (0.74 to 1.01)
Low		1.12 (1.04 to 1.21)	0.85 (0.75 to 0.97)
Very low	1.00		
Extent of pain from RA			
Low	1.00		
High		1.39 (1.19 to 1.63)	1.22 (0.93 to 1.58)
BMI			
Thin (<18.5 kg/m ²)		0.79 (0.70 to 0.90)	1.26 (1.04 to 1.53)
Moderate (18.5kg/m-23.9kg/m ²)	1.00		
Overweight (24.0kg/m-26.9kg/m ²)		1.05 (0.99 to 1.11)	0.95 (0.84 to 1.07)
Obese (≥27.0 kg/m ²)		1.20 (1.11 to 1.29)	1.00 (0.86 to 1.17)

Continued

Table 2 Continued

	RA		
	Appropriate sleeper (7–8 hours)	Short sleeper (≤6 hours)	Long sleeper (≥9 hours)
	Ref	OR 95% CI	OR 95% CI
Year			
2007	1.00		
2008		1.05 (0.89 to 1.24)	1.30 (0.98 to 1.73)
2009		0.95 (0.80 to 1.12)	1.19 (0.90 to 1.57)
2010		1.00 (0.84 to 1.19)	1.22 (0.91 to 1.64)
2011		1.03 (0.86 to 1.23)	1.10 (0.82 to 1.47)
2012		1.00 (0.84 to 1.19)	1.14 (0.85 to 1.54)
2013		1.16 (0.98 to 1.38)	1.04 (0.78 to 1.40)

BMI, body mass index; RA, rheumatoid arthritis.

Table 3 Results of logistic regression between rheumatoid arthritis and sleep duration by extent to pain of rheumatoid arthritis

	RA		
	Appropriate sleeper (7–8 hour)	Short sleeper (≤6 hour)	Long sleeper (≥9 hour)
	Ref	OR 95% CI	OR 95% CI
<i>Extent to pain of rheumatoid arthritis (high)</i>			
RA			
No	1.00		
Yes		1.28 (1.04 to 1.58)	1.40 (0.93 to 2.12)
<i>Extent to pain of rheumatoid arthritis (low)</i>			
RA			
No	1.00		
Yes		0.84 (0.49 to 1.46)	0.52 (0.18 to 1.45)

*Adjusted for all variables

RA, rheumatoid arthritis.

A nationwide study conducted in the USA found that RA is associated with sleep disturbances in ~10 million adults.²² The presence of sleep disturbances in patients diagnosed with a range of rheumatological-related diseases including systemic lupus erythematosus, fibromyalgia, chronic fatigue syndrome, multiple sclerosis and RA have also been assessed.²³ Additionally, recent studies have indicated that sleep disturbances from other causes such as difficulties with the onset of sleep and waking up early in the morning are also major symptoms in patients with RA, and that fatigue in patients with RA is likely due to poor quality of sleep, a functional disability, joint pain and/or depressive symptoms.^{23–27} Poor quality of sleep and sleep disturbances can worsen physical and mental health conditions, including RA symptoms and pain, in the general population.²⁸ Similarly, the pain and discomfort caused by RA with inflammation may result in a greater frequency of sleep disturbances, contributing to functional impairments such as poor sleep quality which have a significantly negative impact on the health and well-being of individuals.²⁹

Along with a significantly higher prevalence of fatigue, there is also a greater risk of sleep disturbances from causes such as obstructive sleep apnoea (OSA) in

patients with RA, because they are more likely to have chronic health issues, including high blood pressure and high BMI. This consequently leads to increased risks of cardiovascular disease and nocturnal sudden cardiac death.³⁰ Accordingly, the autonomic response is more severe in patients with chronic OSA than in individuals with a low risk of OSA.^{30–33}

In the present study, a multinomial logistic regression analysis revealed that the important factors influencing the relationship between RA and sleep duration include perceived stress and the extent of RA pain. Although the causes of sleep disturbances in patients with RA are likely multifactorial, only 30% of older Americans with sleep disturbances seek treatment at hospitals or treatment centres using multidisciplinary approaches, relying on various self-care strategies instead.^{34 35} Therefore, the provision of comprehensive care for patients with RA requires encouraging the patient to report sleep disturbances as well as conducting timely diagnoses to reduce their symptoms. In this manner, the present data regarding the prevalence of sleep disturbances in patients with RA will contribute to the awareness of physicians and healthcare professionals regarding this issue and may aid in the development of appropriate interventions

to properly manage, minimise or eliminate these symptoms.

There are several potential limitations that should be taken into consideration when interpreting the present results. First, because this study used a cross-sectional design, the results may reflect reverse causality and a bidirectional relationship in the association between RA and sleep duration. Therefore, longitudinal studies using validated measures of RA and sleep duration are required to see if these findings can be replicated and to clarify the causality and mechanisms that underlie the association between RA and sleep duration. Second, although the use of self-reports is a valuable source of information in large-scale epidemiological studies, the lack of validated questionnaires assessing RA and sleep duration was a major limitation of the present study, as more objective methods tend to yield more accurate results. Controlling for socioeconomic status, health status and behaviour variables, as in the present study, may partially ameliorate these issues, but future in-depth studies are necessary to determine more accurately the relationship between RA and sleep disturbances, including difficulty falling asleep, difficulty maintaining sleep, time spent in bed, waking after sleep onset, sleep onset latency, sleep quality, time of going to bed in the evening, time of turning out the lights with the intention to sleep, wake time in the morning, time of getting out of bed in the morning and insomnia.

CONCLUSIONS

The present study found that patients with RA may be at a higher risk for sleep disturbances than are individuals without RA. This apparent difference may be attributed to pain reported by patients with RA, which may also be associated with RA itself. The present findings suggest that healthcare professionals who treat patients with RA in routine clinical practice should be aware of the relationship between RA and sleep disturbances. Future research that includes objective measures of sleep disturbances is necessary to fully characterise the extent to which sleep disturbances affect patients with RA.

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